Supporting Information

Expedient Synthesis of Epigoitrin from L-Ascorbic Acid

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(S)-2,2-Dimethyl-1,3-dioxolane-4-carbaldehyde (4). Compound **4** was prepared from *L*-ascorbic acid according to literature reported method.^[15,16] The overall 3 step yield is 50%.

(R)-2,2-Dimethyl-4-vinyl-1,3-dioxolane (5). To an ice cooled solution of potassium *tert*-butoxide (0.96 g, 8.57 mmol) in 10 mL dry THF was added methyltriphenylphosphonium bromide (3.06 g, 8.57 mmol) under nitrogen atmosphere. The solution was stirred for 1.5 h, then compound **4** (1.01 g, 7.79 mmol) in 5 mL THF was added and the stirring was continued for another 3 h. The reaction was quenched by adding 3 mL water. The mixture was extracted with ether (15 mL × 3). The combined organic phase was washed with brine, dried over anhydrous MgSO₄, concentrated at ambient pressure to remove the ether. The residue was distilled under reduced pressure (50 mm) at 50°C to afford **5** as an oil, 738 mg (4.21 mmol, 74%). The ¹H NMR is consistent with literature.^[16] ¹H NMR (400 MHz, CDCl₃) δ 5.80 (m, 1H), 5.33 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 10.3 Hz, 1H), 4.48 (m, 1H), 4.08 (t, *J* = 7.1 Hz, 1H), 3.58 (t, *J* = 7.9 Hz, 1H), 1.41 (s, 3H), 1.38 (s, 3H).

(R)-But-3-ene-1,2-diol (6). To a stirred solution of **5** (12 mg, 93.63 μmol) in 1.5 mL absolute MeOH was added *p*-toluenesulfonic acid (17.2 mg, 100 μmol) at 0°C. The reaction was then allowed to warm up to ambient temperature and stirred for another 12 h. It was concentrated in vacuo, the residue was subjected to silica gel flash chromatography (PE: EtOAc = 2:1) to afford **6** as a colorless oil, 7.9 mg (89.5 μmol, 96%). ¹H NMR (400 MHz, CDCl₃) δ 5.82 (ddd, *J* = 15.7, 10.9, 5.0 Hz, 1H), 5.33 (d, *J* = 17.3 Hz, 1H), 5.24 – 5.15 (d, *J* = 17.3 Hz, 1H), 4.23 (s, 1H), 3.68 – 3.41 (m, 3H), 3.20 (s, 1H).

(R)-2-Hydroxybut-3-enyl 4-methylbenzenesulfonate (7). To a stirred solution of compound **6** (54 mg, 613 μmol) and anhydrous pyridine (0.3 mL, 3.68 mmol) in 2 mL dry DCM was added tosylchloride (117 mg, 613 μmol). The reaction mixture was stirred for 12 h. The reaction was quenched with 3 mL saturated NaHCO₃ aqueous solution, extracted with DCM (10 mL × 3). The pyridine was removed by washing with sat. CuSO₄ aqueous solution (3 × 5 mL). The organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (PE : EtOAc = 10:1) to give **7** as a white solid, 95 mg (466 μmol, 76%). $[\alpha]_D^{25} = +11^\circ$ (c=1, acetone), ¹H NMR^[16] (400 MHz, CDCl₃) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 5.74 – 5.71 (m, 1H),

5.36 (d, $J = 17.2$ Hz, 1H), 5.24 (t, $J = 8.5$ Hz, 1H), 4.38 (s, 1H), 4.05 (dd, $J = 10.1, 3.4$ Hz, 1H), 3.90 (dd, $J = 10.1, 7.5$ Hz, 1H), 2.44 (s, 3H).

(R)-2-(2-Hydroxybut-3-enyl)isoindoline-1,3-dione (8). A mixture of potassium phthalimide (46 mg, 247.7 μmol) and compound **7** (30 mg, 123.9 μmol) was dissolved in 1.0 mL DMF. The reaction mixture was heated to reflux overnight. The reaction was quenched with 2 mL water, and the aqueous solution was extracted with diethyl ether (3×5 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to silica gel flash chromatography (PE: EtOAc = 10:1) to give compound **8** as yellow solid, 23 mg (109 μmol , 88%). $[\alpha]_D^{25} = -2^\circ$ ($c = 1$, DCM) ^1H NMR (300 MHz, CDCl_3): 7.86 (d, $J = 6.0$ Hz, 2H), 7.74 (d, $J = 6.0$ Hz, 2H), 5.94 (ddd, $J = 17.2, 10.3, 7.0$ Hz, 1H), 5.40 (d, $J = 17.1$ Hz, 1H), 5.22 – 5.19 (m, 1H), 4.47 (m, 1H), 3.86 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 169.32, 137.82, 134.65, 132.39, 123.96, 117.32, 71.71, 44.31. HRMS calcul. for $[\text{M}+\text{Na}^+]$: 240.0631, found $[\text{ESI}^+]$: 240.0633; error 0.92 ppm.

(R)-5-vinyloxazolidine-2-thione (Epigoitrin). To a solution of MeNH_2 in EtOH (27-32% w/w, 0.5 mL) was added compound **8** (30 mg, 0.138 mmol). The mixture was stirred at ambient temperature for 12 h and a large amount of white solid was formed. The precipitation was filtrated and the crude product **9** was directly used for the next step reaction. Compound **9** was dissolved in 1.0 mL dry THF, TCDI (thiocarbonyl diimidazole) (24.6 mg, 138 μmol) was added. The reaction mixture was stirred at ambient temperature for 1 h, and was concentrated, the residue was subjected to silica gel flash chromatography (PE: EtOAc = 8:1) to give epigoitrin as white solid, 12 mg (93.02 μmol , 70%). $[\alpha]_D^{23.1} = +71^\circ$ ($c = 1$, CHCl_3), reported $[\alpha]_D^{23.1} = +71^\circ$ ($c = 1$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 8.23 (br, 1H), 5.94 (ddd, $J = 17.2, 10.3, 7.0$ Hz, 1H), 5.46 (d, $J = 17.1$ Hz, 1H), 5.36 (d, $J = 10.4$ Hz, 1H), 5.31 – 5.28 (m, 1H), 3.92 (t, $J = 9.4$ Hz, 1H), 3.53 (t, $J = 9.4$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 189.61, 132.90, 120.57, 83.35, 49.06. HRMS calcul. for $[\text{M}+\text{H}]^+$: 130.0321, found $[\text{ESI}^+]$: 130.0330; error 6.97 ppm.

Compound 4. ^1H NMR (400 MHz, CDCl_3) δ 9.72 (d, $J = 1.4$ Hz, 1H), 4.39 (ddd, $J = 6.0, 4.1, 2$ Hz, 1H), 4.17 (dd, $J = 8.7, 4.7$ Hz, 1H), 4.10 (dd, $J = 8.7, 4.7$ Hz, 1H), 1.47 (s, 3H), 1.42 (s, 3H).

Compound 5. ^1H NMR (400 MHz, CDCl_3) δ 5.80 (m, 1H), 5.33 (d, $J = 17.1$ Hz, 1H), 5.20 (d, $J = 10.3$ Hz, 1H), 4.48 (m, 1H), 4.08 (t, $J = 7.1$ Hz, 1H), 3.58 (t, $J = 7.9$ Hz, 1H), 1.41 (s, 3H), 1.38 (s, 3H).

Compound 6. ^1H NMR (400 MHz, CDCl_3) δ 5.82 (ddd, $J = 15.7, 10.9, 5.0$ Hz, 1H), 5.33 (d, $J = 17.3$ Hz, 1H), 5.21 – 5.18 (d, $J = 17.3$ Hz, 1H), 4.23 (s, 1H), 3.65 – 3.44 (m, 3H), 3.20 (s, 1H).

Compound 7. ^1H NMR^[16] (400 MHz, CDCl_3) δ 7.79 (d, $J = 8.1$ Hz, 2H), 7.35 (d, $J = 7.9$ Hz, 2H), 5.74 – 5.71 (m, 1H), 5.36 (d, $J = 17.2$ Hz, 1H), 5.24 (t, $J = 8.5$ Hz, 1H), 4.38 (s, 1H), 4.05 (dd, $J = 10.1$, 3.4 Hz, 1H), 3.90 (dd, $J = 10.1$, 7.5 Hz, 1H), 2.44 (s, 3H).

Compound 8. ^1H NMR (300 MHz, CDCl_3): 7.86 (d, $J = 6.0$ Hz, 2H), 7.74 (d, $J = 6.0$ Hz, 2H), 5.94 (ddd, $J = 17.2, 10.3, 7.0$ Hz, 1H), 5.40 (d, $J = 17.1$ Hz, 1H), 5.22 – 5.19 (m, 1H), 4.47 (m, 1H), 3.86 (m, 2H).

^{13}C NMR spectrum of compound **8** ^{13}C NMR (75 MHz, CDCl_3) δ 169.32, 137.82, 134.65, 132.39, 123.96, 117.32, 71.71, 44.31.

HRMS of compound **8**

Sample Name	j-1-79	Position	Vial 1	Instrument Name	Instrument 1	User Name	
Inj Vol	0	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	j-1-79-01.d	ACQ Method		Comment		Acquired Time	6/26/2012 9:09:53 AM

¹H NMR spectrum of epigoitrin ¹H NMR (300 MHz, CDCl₃) δ 8.23 (br, 1H), 5.94 (ddd, *J* = 17.2, 10.3, 7.0 Hz, 1H), 5.46 (d, *J* = 17.1 Hz, 1H), 5.36 (d, *J* = 10.4 Hz, 1H), 5.31 – 5.28 (m, 1H), 3.92 (t, *J* = 9.4 Hz, 1H), 3.53 (t, *J* = 9.4 Hz, 1H).

^{13}C NMR spectrum of epigoitrin ^{13}C NMR (101 MHz, CDCl_3) δ 189.61, 132.90, 120.57, 83.35, 49.06.

HRMS of epigoitrin

Sample Name	jj-1-90-2	Position	Vial 1	Instrument Name	Instrument 1	User Name	
Inj Vol	0	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	jj-1-90-2-02.d	ACQ Method		Comment		Acquired Time	7/13/2012 3:47:20 PM